REMARKS/ARGUMENTS

Claims 92, 93, 96-99, 104-106 and 121-135 are pending in the present application.

Applicants note the Examiner's comment that submission of a new Abstract is required because the present Abstract is not clearly indicative of the invention to which the claims are directed and state herewith that they will present a new Abstract upon indication of allowable claims by the Examiner.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH

The Examiner rejected claims 92-93, 96-99, 104-106 and 122-135 under 112, first paragraph as allegedly not being enabled. In this regard, the Examiner has alleged that undue experimentation would be required to determine all species of exendin analogs that could be derivatized with a lipophilic substituent as presently claimed:

"The effects of this [changes to the amino acid sequence of exendin-4] are unknown for the reasons of record, and as such, when this variable is added, the claimed invention becomes little more than conjecture. Moreover, without guidance, the changes which can be made in the peptide/protein structure and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessary, and improperly extensive and undue" (page 5 of Office Action, citing to Amgen Inc. v. Chugai Pharmaceutical Co. Ltd, 927 F2d, 18 USPQ 2d 1016 (Fed. Cir. 1991))).

Applicants respectfully traverse this rejection.

The law is clear that patent applicants are not required to disclose every species that may be encompassed by their claims even in an unpredictable art In re Wands, 8. USPQ 1400, 1404 (Fed. Cir. 1988). Further, it is not required that every embodiment be operative in order to be enabling under section 112, first paragraph Atlas Powder Co. v. E.I. Dupont de Nemours & Co. 224 USPQ 409 (Fed. Cir. 1984). Nowhere does the Examiner address these fundamental principles.

The Examiner has also erred in ignoring and/or failing to consider and appreciate the evidence provided by Applicants in the Amendment filed December 23, 2004. Specifically, Applicants cited to US provisional application 60/065,442 filed November 14, 1997 (copy provided in Amendment filed December 23, 2004) and AU 731732 (copy provided in Amendment filed December 23, 2004) in the December 23, 2004 Amendment as providing evidence that as of the present application's earliest priority filing date of February 27, 1998, numerous exendin analogs which retain biological activity had been identified as had specific substitutions that could be made at specific residues of exendin-4.

US provisional application 60/065,442[1] disclosed over 50 analogs of exendin-4 (see Figure 4) and presented data for 22 of these analogs showing that they produced a % drop in blood glucose levels in mice that was comparable to or better than that produced by exendin-4 (see Table III on page 72).

AU 731732 (copy attached), which is an English language counterpart of WO 97/46584 published December 11, 1997, described mutations that could be made at amino acids 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 13, 14, 22, 23, 25, 26, 27 and 30 of exendin-4 (see pages 6-7 of the application) and still retain the insulinotropic activity of exendin-4.

Thus, regardless of whether the Examiner had made a prima facie case of nonenablement, Applicants had more than sufficiently rebutted it by the above evidence that it was known which residues in exendin-4 could be changed to produce exendin-4 analogs that stimulate insulin release and that specific analogs had been described. Further, as

1 It was noted in the December 23, 2004 Amendment that 60/065,442 was incorporated by reference in WO 98/03231 because pursuant to 37 CFR 1.14, provisional applications incorporated by reference in a PCT publication are available to the public and since WO 98/03231 published on July 16, 1998, the provisional application would have been available to the public on or about that date. (Applicants were thus not engaging in "improper incorporation of references" as alleged by the Examiner on page 8 of the present Office Action but rather, were properly providing evidence that the state of the art with respect to exendin analogs was advanced as of the priority filing date of the present application.

admitted by the Examiner, methods for identifying further exendin analogs were known in the prior art[2].

The Examiner's position is further unsound in view of the fact that a patent "need not teach and preferably omits what is well known in the art" [Hybritech, Inc. v. Monoclonal Antibodies Inc., 231 USPQ 81, 94 (Fed. Cir. 1986) cert. denied, 480 U.S. 947 (1987), see also Ajinomoto Co. Inc. v. Archer Daniels Midland Co., 56 USPQ2d 1332, 1338 (Fed Cir. 2000) "Requiring inclusion in the patent of known scientific/technological information would add an imprecise and open-ended criterion to the content of patent specifications, could greatly enlarge the content of patent specifications and unnecessarily increase the cost of preparing and prosecuting patent and could tend to obfuscate rather than highlight the contribution to which the patent is directed. A patent is not a scientific treatise, but a document that presumes a readership skilled in the field of the invention."].

Indeed, the provision of documents showing what one skilled in the art knew at the time of the filing of an application are appropriately considered during prosecution to support enablement (see MPEP 2164.05).

In addition, further evidence that the experimentation necessary to determine those changes can be made in the exendin-4 sequence is provided by WO 98/05351 (copy attached), published February 12, 1998 (i.e., before the present application's earliest priority filing date of February 27, 1998) which discloses numerous exendin agonists of formula I (see page 6 of WO 98/05351). It is Applicants' position that this publication, together with the previously discussed evidence (US provisional application 60/065,442, US patent 5,424,586 and AU 731732) showing that specific exendin analogs and methods for identifying further such analogs were known as of the present application's earliest priority filing date of February 27, 1998 clearly demonstrates that pending claims 92-94, 96-99, 104-106 and 121-135 are fully enabled by the present application as well as knowledge in the art.

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2 Eng US patent 5,424,286 was previously cited by the Examiner as providing a means for identifying any specific mammalian analogs of exendin-4 (see page 10 of June 28, 2004 Office Action).

Indeed, it is Applicants' position that if the Examiner properly considers the aforementioned evidence, he must reach a conclusion that the present claims are fully enabled.

For example, the Examiner has previously cited articles showing that the effects of changes on protein structure on biological activity are generally unpredictable and has cited in the present Office Action to the Amgen case as supporting his assertion that the experimentation necessary to identify such changes is improperly undue. However, neither of these assertions is on point.

With respect to the articles showing that the effects of changes on protein structure on biological activity are generally unpredictable, Applicants submit that as applied to exendin agonists this is an inaccurate characterization because as demonstrated by US provisional application 60/065,442, by AU 731732 and by WO 98/05351, the exendin-4 agonist art was well developed as of the priority filing date of the present application. The Examiner thus mischaracterized the state and level of the art in **this** field. One of skill in the art clearly had available many known exendin-4 analogs at the time of filing of the present application and even if such analogs were exhausted, would have been well positioned to generate other such analogs given the existing technology platform.

Turning to Amgen, this case can clearly be distinguished from the present application on at least four grounds:

1) in Amgen, the rejected claim was to analogs of a 165 amino acid protein called erythropoietin or EPO; in the present application, exendin-4 is 39 amino acids in length

2) in Amgen, the rejected claim contained no limitation on the number of substitutions that could be made in the sequence; in the present claims, the maximum number of substitutions that can be made in the exendin-4 sequence is ten (claim 92), six (claim 93) or four (claim 127).

3) in Amgen, the head of Amgen's EPO analog program did not know whether the 50-80 analogs tested by Amgen had the requisite biological activity; here, numerous exendin-4 analogs were known as of the priority filing date and US provisional application 60/065,442

presented data showing that the 22 analogs tested produced a % drop in blood glucose levels in mice that was comparable to or better than that produced by exendin-4 (see Table III on page 72).

4) in Amgen, the court noted that after five years of experimentation, Amgen was unable to specify which analogs have the claimed biological properties; here, specific exendin analogs were known as of the present application's earliest priority filing date of February 27, 1998 (see US provisional application 60/065,442, AU 731732, and WO 98/05351) and subsequent to that date, other analogs could be (and have been) readily identified.

Accordingly, in view of the above arguments and evidence, it is clear that the present claims are clearly enabled and withdrawal of this rejection is therefore respectfully requested.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. 112, SECOND PARAGRAPH

The Examiner rejected claim 96 as depending upon cancelled claim 94.

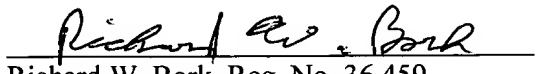
In reply, Applicants submit this rejection is rendered moot by the amendment to claim 96 presented herein.

The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Please charge any deficiencies or overpayment to Deposit Account No.14-1447.

Respectfully submitted,

Date: April 28, 2006



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